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Development of Catalysts for the Stereoselective Hydrogenation of α,β-Unsaturated Ketones

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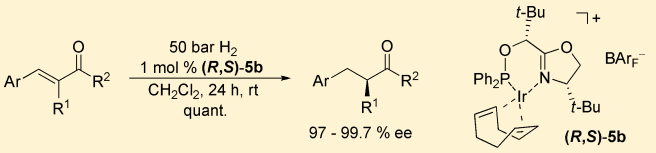
Supporting Information

ABSTRACT: Iridium phosphinitoxazoline complexes were found to be new efficient catalysts for the asymmetric hydrogenation of arylated α,β-unsaturated ketones. Linear as well as cyclic substrates are hydrogenated with similar success, giving selectivities of up to 99.7% ee.



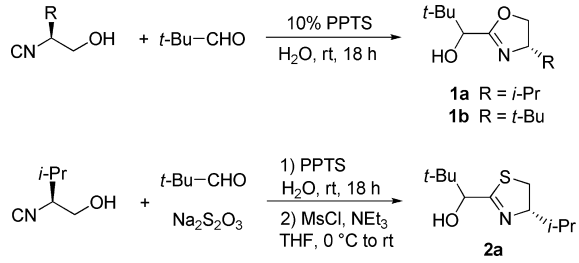
Asymmetric hydrogenations belong to the most important catalytic processes for the synthesis of optically active compounds. Their high efficiency, ecofriendliness, and cost–benefit ratio made them one of the best investigated methods in the last 40 years.[1] The homogeneous hydrogenation of functionalized alkenes containing an additional coordinating group (except the alkene) started in 1965 with the rhodium catalyst $Rh(PPh_3)_3Cl$, developed by Wilkinson[2,3] and Coffey.[4] First asymmetric versions were reported two years later independently by Horner[5] and Knowles.[6] In 1977, Knowles introduced the bidentate *P*-stereogenic phosphine ligand DIPAMP, which allowed the stereoselective hydrogenation of α-acylaminoacrylates with up to 96% ee.[7] This process was used as a key step in the synthesis of Dopa, the first industrially applied asymmetric hydrogenation.[8,9] In the meantime, a wide range of other ligands have been developed for not only Rh- but also Ru-catalyzed processes.[10−14] Nevertheless, the asymmetric hydrogenation of nonfunctionalized alkenes was a challenge for a long time.[15]

In 1977, Crabtree described the first homogeneous achiral iridium catalyst which allowed the reduction of a wide range of unfunctionalized, also highly substituted, alkenes.[16,17] On the basis of this pioneering work, Pfaltz et al. developed a new class of hydrogenation catalysts, based on bidentate *P*,*N*-ligands, the so-called PHOX ligands.[18,19] These ligands gave already excellent selectivities in various Pd-catalyzed reactions, such as allylic alkylations or Heck reactions.[20−23] The Ir complexes were highly active in the asymmetric hydrogenation of unfunctionalized alkenes, providing excellent ee's.[24] During the past decade, the family of the PHOX and related ligands improved significantly, and today a wide range of unfunctionalized alkenes can be hydrogenated with up to 99% ee.[25−34]

In 2008, Bolm[35,36] and Hou[37,38] more or less simultaneously reported that the Ir-catalyzed enantioselective hydrogenation is also a suitable protocol for the stereoselective synthesis of α-substituted chiral ketones. In addition, the best results were obtained with the PHOX ligand. Linear as well as cyclic ketones gave selectivities of up to 99% ee.

Our group is also involved in the development of new ligands and catalysts for asymmetric reactions. Recently, we reported an easy and highly flexible protocol for the synthesis of 2-(1-hydroxyalkyl)oxazolines **1**.[39] These can be obtained by a Passerini-type reaction of hydroxyisonitriles[40] and aldehydes such as pivaldehyde (Scheme 1). The products are obtained as a mixture of diastereomers, which can easily be separated by flash chromatography. The (*S*,*S*)-isomers were found to be excellent ligands for stereoselective additions of alkyl- and arylzinc reagents toward aldehydes (up to 98% ee). A strong nonlinear effect could be observed in these reactions.[41]

Scheme 1. Syntheses of 2-(1-Hydroxyalkyl)oxazolines and -thiazolines



The analogous thiazoline derivatives **2** can be obtained in an analogous manner in the presence of $Na_2S_2O_3$.[42,43] In this case, the cyclization toward the heterocycle does not proceed automatically but requires an activation of the hydroxyl functionality. This allowed us to get access, e.g., to **2a**, the *S*-analogue ligand to **1a**.[41]

Reaction with chlorophosphine and phosphite bidentate *P*,*N*-ligands should be easily accessible and applicable to a wide range of asymmetric reactions. The free choice of the chlorophosphines and the modular approach toward the heterocyclic alcohols should allow the generation of libraries of interesting ligand candidates in a straightforward manner.

As a showcase, we synthesized the diphenylphosphinites **3** and **4** (table 1). These compounds were found to be sensitive to hydrolysis and oxidation, and therefore, the workup should be carried out under inert conditions. This fact might also

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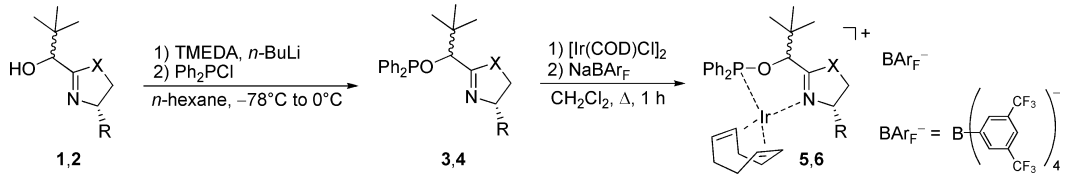
Table 1. Syntheses of New Iridium Complexes As Potential Hydrogenation Catalysts



entry	oxazoline/thiazoline	R	X	phosphinite	yield (%)	Ir complex	yield (%)
1	(*R*,*S*)-**1a**	*i*-Pr	O	(*R*,*S*)-**3a**	57	(*R*,*S*)-**5a**	97
2	(*S*,*S*)-**1a**	*i*-Pr	O	(*S*,*S*)-**3a**			
3	(*R*,*S*)-**1b**	*t*-Bu	O	(*R*,*S*)-**3b**	62	(*R*,*S*)-**5b**	93
4	(*S*,*S*)-**1b**	*t*-Bu	O	(*S*,*S*)-**3b**			
5	(*R*,*S*)-**2a**	*i*-Pr	S	(*R*,*S*)-**4a**	49	(*R*,*S*)-**6a**	80
6	(*S*,*S*)-**2a**	*i*-Pr	S	(*S*,*S*)-**4a**	42	(*S*,*S*)-**6a**[a]	80[a]

[a]This compound proved to be unstable and decomposed in a few days.

explain the moderate isolated yields of the posphinites (42−62%), although the conversion was clean and complete. Interestingly, no reactions were observed with the (*S*,*S*)-configured oxazoline derivatives **1**, while the (*R*,*S*)-isomers gave rise to the derived products **3**. In the case of the thiazoline **2a**, both isomers reacted to give the phosphinites **4a** in comparable yields.

Unfortunately, the phosphinites could not be stored for a longer time, and this forced us to convert them directly into the corresponding Ir complexes **5** and **6** by heating a CH_2Cl_2 solution with $[Ir(COD)Cl]_2$ for 1 h. Subsequently, the counterion chloride was replaced by BAr_F^- [tetrakis[3,5-bis(trifluoromethyl)phenyl]borate] to get air- and moisture-stable complexes.[44,45] We were pleased to see that these colored complexes are stable compounds which could be purified easily by flash chromatography. On crystallization, all complexes gave orange-red crystals which were suitable for X-ray structure analysis (Figure 1, ORTEP plots of all complexes

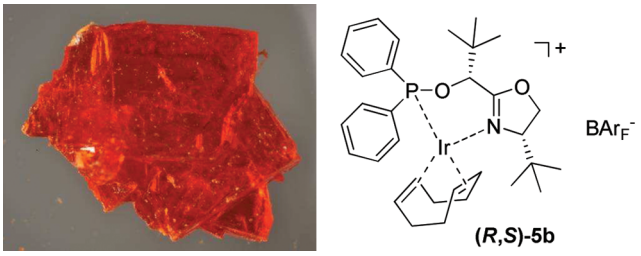


Figure 1. Iridium complex (*R*,*S*)-**5b**.

will be found in the Supporting Information). And indeed, as expected, both the (*R*,*S*)-oxazolines **5** and the (*R*,*S*)-thiazoline **6a** coordinate toward the iridium as bidentate *P*,*N*-ligand. Interestingly, the Ir complex of (*S*,*S*)-**6a** could not be crystallized, and the complex decomposed in a few days.

The Ir complexes obtained were subsequently used as catalysts for asymmetric hydrogenations of unsaturated substrates. Because it was not clear which substance class is best suited for our new catalysts, we decided to investigate a wide range of substrates (Figure 2) such as α-hydroxy ketones (**A**), phosphinates (**B**), substituted cinnamates (**C**) and cinnamyl alcohols (**D**), enamides (**E** and **F**), α-amino acrylates (**G**), and α,β-unsaturated ketones (**H**). We chose substrates which could easily be analyzed by GC on chiral phase. Interestingly, no reaction was observed with substrate classes

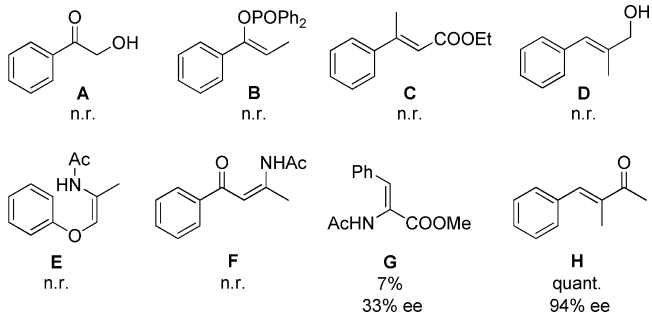


Figure 2. Substrate classes investigated in catalytic hydrogenations (ee's given for catalyst (*R*,*S*)-**5a**).

A−**F**, even after 24 h at a H_2 pressure of 50 atm and a catalyst loading of up to 3 mol %. The unsaturated amino acid derivative **G** showed a very slow conversion (7%), and the ee was low. By far the best result was obtained with the α,β-unsaturated ketone **H**, which provided the (*S*)-configured α-chiral ketone with 94% ee (with catalyst (*R*,*S*)-**5a**) in a perfect yield.

Therefore, we tested our new catalysts in the hydrogenation of substrates of type **H** (Table 2). Independent of the substitution pattern and the catalyst used, all substrates showed almost complete conversion. With linear ketones **7a**−**f** the valine-derived ligand (*R*,*S*)-**5a** gave high ee's in the range of 95 ± 2%, which could even be improved by switching to the sterically more hindered *tert*-leucine ligand (*R*,*S*)-**5b** (entries 1−6). Except for the *ortho*-substituted arylated ketone **7f** (entry 6) all substrates gave ee's >99% with quantitative conversion. The oxazoline ligands **5** proved to be superior to the thiazoline analogue (*R*,*S*)-**6a**. Although a good conversion was observed, the ee's found with the same substrates were only in the range of 65−81%. This effect was even more dramatic when we investigated another class of the substrates, unsaturated cyclohexanone derivatives (entries 7−9). Here, with the thiazoline complex (*R*,*S*)-**6a** the ee's dropped to 29−51%, while oxazoline catalyst (*R*,*S*)-**5b** still gave excellent selectivities of 98 ± 1% ee.

For the screening of our catalysts we used rather high H_2 pressures and long reaction times to guarantee a complete conversion of our substrates. To get an impression of the reactivity of our catalysts and to figure out if chlorinated solvents such as CH_2Cl_2 are required, we also changed the reaction parameters. Using ketone **7h** as a model substrate, we

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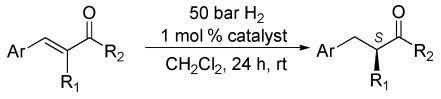
Table 2. Asymmetric Hydrogenations of α,β-Unsaturated Ketones 7

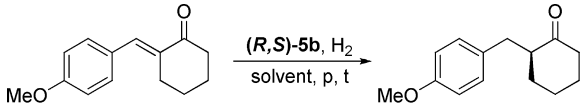


7 8

						(*R*,*S*)-5a		(*R*,*S*)-5b		(*R*,*S*)-6a	
entry	7	Ar	R^1	R^2	product	conv (%)	ee (%)	conv (%)	ee (%)	conv (%)	ee (%)
1	**7a**	Ph	Me	Me	**8a**	>99	94	>99	99.4	>99	71
2	**7b**	Ph	Me	Et	**8b**	>99	97	>99	99.1	>99	81
3	**7c**	Ph	Et	Me	**8c**	96	93	>99	99.7	96	75
4	**7d**	4-MeO-Ph	Me	Me	**8d**	>99	94	>99	99.1	>99	65
5	**7e**	4-Me-Ph	Me	Me	**8e**	98	94	99	99.5	98	68
6	**7f**	2-Me-Ph	Me	Me	**8f**	92	95	>99	98	88	73
7	**7g**	Ph	$-(CH_2)_4-$		**8g**	>99	92	>99	99	>99	42
8	**7h**	4-MeO-Ph	$-(CH_2)_4-$		**8h**	>99	90	>99	97	>99	29
9	**7i**	2-Me-Ph	$-(CH_2)_4-$		**8i**	>99	93	>99	98	>99	51

analyzed the conversion by dependence of the pressure and the solvent used (Table 3). Under the reaction conditions described, the hydrogenation was complete after 2 h (entry 1). Toluene might be a suitable substitute. Although the hydrogenation is not as fast as in CH_2Cl_2 (80% conversion after 2 h), it was also complete after 4 h (entry 2). In EtOAc, the reaction is much slower (entry 3), and EtOH and dioxane are completely unsuitable (entries 4 and 5). CH_2Cl_2 seems to be the solvent of choice. Even at a lower H_2 pressure of 20 atm, the reaction was complete after 2 h (entry 6). In principle, a Parr apparatus can be used for hydrogenation, although the reaction slows down significantly. At 5 atm H_2 it takes 8 h for completion (entry 7), and at 1 atm only 35% conversion was observed after 24 h (entry 8). It should be mentioned that the ee value was unchanged, even in toluene as solvent.

Table 3. Influence of the Reaction Parameters on the Reaction Rate



7h 8h

entry	solvent	pressure (atm)	time (h)	conv (%)
1	CH_2Cl_2	50	2	>99
2	toluene	50	4	>99
3	EtOAc	50	24	60
4	EtOH	50	24	traces
5	dioxane	50	24	–
6	CH_2Cl_2	20	2	>99
7	CH_2Cl_2	5	8	>99
8	CH_2Cl_2	1	24	35

CONCLUSION

In conclusion, we could show that phosphinitoxazolines **3** are new efficient ligands for Ir-catalyzed asymmetric hydrogenations of arylated α,β-unsaturated ketones. By far, the best results are obtained with the *tert*-leucine-derived ligand (*R*,*S*)-**5b**, which gives excellent ee's with linear as well as cyclic substrates. By varying the central metal and the substitution pattern, especially at the phosphorus atom, a wide range of comparable complexes and catalysts are accessible, which should be useful for not only asymmetric hydrogenations but also many other transition-metal-catalyzed reactions. Investigations of such complexes are currently in progress.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of the Phosphinitoxazolines 3 and -thiazoline 4. The corresponding oxazoline[39] or thiazoline[41] (*n* mmol) was dissolved in dry hexanes (10*n* mL), and TMEDA (1.3*n* mmol) was added at room temperature. The solution was cooled to −78 °C before *n*-butyllithium (1.3*n* mmol, 1.6 M in hexanes) was added. The mixture was stirred for 15 min at −78 °C and further 60 min at 0 °C. Then chlorodiphenylphosphine (1.3*n* mmol) was added, and the solution was stirred at room temperature. After the reaction was complete, the solid was filtered off and the solvent was evaporated in vacuo. The residue was purified by flash chromatography on SiO_2 (hexanes/diethylether/triethylamine). The ligands were found to be highly sensitive toward air and moisture and where therefore directly converted into the corresponding Ir complexes.

(*S*)-2-[(*R*)-1-[(Diphenylphosphino)oxy]-2,2-dimethylpropyl]-4-isopropyl-4,5-dihydrooxazole [(*R*,*S*)-3a]: 57% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76 (d, J = 6.8 Hz, 3 H), 0.87 (d, J = 6.8 Hz, 3 H), 1.02 (s, 9 H), 1.55 (qqd, J = 6.8, 6.8, 6.5 Hz, 1 H), 3.69 (dd, J = 8.8, 8.1 Hz, 1 H), 3.79 (ddd, J = 9.6, 8.8, 6.5 Hz, 1 H), 4.14 (dd, J = 9.6, 8.1 Hz, 1 H), 4.29 (d, J = 9.0 Hz, 1 H), 7.29−7.35 (m, 6 H), 7.49−7.54 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 19.1, 26.2, 32.2, 35.5 (d, J = 6.0 Hz), 69.6, 71.7, 83.6 (d, J = 19.3 Hz), 127.9 (d, J = 6.7 Hz), 128.2 (d, J = 7.2 Hz), 128.9, 129.3, 130.4 (d, J = 21.6 Hz), 130.8 (d, J = 22.7 Hz), 142.0 (d, J = 16.9 Hz), 142.5 (d, J = 18.3 Hz), 165.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 117.0. On the basis of the instability of this compound, no acceptable elemental analysis and HRMS data could be obtained.

(*S*)-4-*tert*-Butyl-2-[(*R*)-1-[(diphenylphosphino)oxy]-2,2-dimethylpropyl]-4,5-dihydrooxazole [(*R*,*S*)-3b]: 62% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (s, 9 H), 1.02 (s, 9 H), 3.79 (dd, J = 9.4, 9.2 Hz, 1 H), 3.85 (dd, J = 9.4, 7.9 Hz, 1 H), 4.12 (dd, J = 9.2, 7.9 Hz, 1 H), 4.31 (d, J = 9.0 Hz, 1 H), 7.27−7.36 (m, 6 H), 7.48−7.55 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 26.3, 33.3, 35.6, 68.4, 75.3, 83.7, 127.9 (d, J = 6.6 Hz), 128.2 (d, J = 7.3 Hz), 128.8, 129.4, 130.2 (d, J = 21.3 Hz), 131.0 (d, J = 22.9 Hz), 142.0, 142.4, 165.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ 116.5. On the basis of the instability of this compound, no acceptable elemental analysis and HRMS data could be obtained.

(*S*)-2-[(*R*)-1-[(Diphenylphosphino)oxy]-2,2-dimethylpropyl]-4-isopropyl-4,5-dihyrothiazole [(*R*,*S*)-4a]: 49% yield; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, J = 6.8 Hz, 3 H), 0.97 (d, J = 6.8 Hz, 3 H), 1.01 (s, 9 H), 2.00 (qqd, J = 6.8, 6.8, 5.8 Hz, 1 H), 2.79 (dd, J = 10.6, 9.3 Hz, 1 H), 3.11 (dd, J = 10.6, 8.8 Hz, 1 H), 4.11 (ddd, J = 9.3, 8.8, 5.8 Hz, 1 H), 4.40 (d, J = 10.3 Hz, 1 H), 7.29−7.37 (m, 6 H), 7.52−7.57 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 19.8,

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26.5, 32.2, 35.8, 35.8 (d, J = 5.9 Hz), 87.2, 87.4 (d, J = 17.6 Hz), 127.9 (d, J = 6.7 Hz), 128.2 (d, J = 7.3 Hz), 128.9, 129.5, 130.6 (d, J = 21.7 Hz), 131.2 (d, J = 23.0 Hz), 141.8 (d, J = 19.2 Hz), 142.2 (d, J = 17.0 Hz), 170.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 115.9. On the basis of the instability of this compound, no acceptable elemental analysis and HRMS data could be obtained.

Preparation of the Iridium Complexes. To a solution of n mmol of the *P*,*N*-ligand in dry dichloromethane (10n mL) $[Ir(COD)Cl]_2$ (0.5n mmol) were added at room temperature. The mixture was refluxed for 1 h and cooled to room temperature. Sodium tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate (1.1n mmol) and H_2O (10n mL) were added, and the mixture was stirred for 30 min. The aqueous layer was extracted with dichloromethane, and the combined organic layers were washed with H_2O and brine and dried over Na_2SO_4. The solvent was evaporated in vacuo, and the crude product was purified by flash chromatography on SiO_2 (dichloromethane).

[(η^4-1,5-Cyclooctadiene)-[(*S*)-2-[(*R*)-1-((diphenylphosphino)-oxy)-2,2-dimethylpropyl]-4-isopropyl-4,5-dihydrooxazole]-iridium(I)] tetrakis[3,5-bis(trifluoromethyl)phenyl]borate [(*R*,*S*)-5a]: 97% yield; red-orange crystals (crystallized from EtOH, mp 163−164 °C); $[\alpha]_D^{20}$ +1.8 (c = 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.25 (d, J = 6.7 Hz, 3H), 0.80 (d, J = 7.0 Hz, 3H), 1.07 (s, 9H), 1.61 (m, 1H), 1.74−1.93 (m, 2H), 2.07 (m, 2H), 2.53−2.34 (m, 4H), 2.85 (m, 1H), 3.51 (m, 1H), 3.95 (dd, J = 4.3, 3.7 Hz, 1H), 4.39 (dd, J = 9.8, 3.7 Hz, 1H), 4.54 (dd, J = 9.8, 4.3 Hz, 1H), 4.74 (d, J = 9.6 Hz, 1H), 4.94 (m, 1H), 5.31 (m, 1H), 7.31 (m, 2H), 7.45 (m, 2H), 7.49−7.61 (m, 8H), 7.72−7.78 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2, 18.3, 25.9, 26.4, 29.1, 31.6, 32.4, 35.4, 35.5, 63.4, 66.3, 68.9, 71.0, 82.4, 98.1, 100.3, 117.5, 124.6 (J = 272.3 Hz), 128.9 (J = 2.7 Hz), 129.0 (J = 10.9 Hz), 129.4 (J = 11.4 Hz), 130.3, 130.9, 131.3 (J = 12.1 Hz), 132.3 (J = 13.7 Hz), 132.8 (J = 2.0 Hz), 133.0 (J = 2.4 Hz), 134.8, 161.7 (J = 49.7 Hz), 172.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 109.3; ^{19}F NMR (376.5 MHz, $CDCl_3$) δ − 62.8 ppm; HRMS (CI) m/z calcd for $C_{31}H_{42}IrNO_2P$ (M − BAr_F)$^+$ 684.2577, found 684.2581. Anal. Calcd for $C_{63}H_{54}BF_{24}IrNO_2P$: C, 48.91; H, 3.52; N, 0.91. Found: C, 49.07; H, 3.22; N, 0.85.

[(η^4-1,5-Cyclooctadiene)-[(*S*)-4-*tert*-butyl-2-[(*R*)-1-((diphenylphosphino)oxy)-2,2-dimethylpropyl]-4,5-dihydrooxazole]iridium(I)] tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate [(*R*,*S*)-5b]: 93% yield; orange crystals (crystallized from Et_2O/hexanes, mp 178−179 °C); $[\alpha]_D^{20}$ +20.0 (c = 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72 (s, 9H), 1.08 (s, 9H), 1.56 (m, 1H), 1.76 (m, 1H), 2.03 (m, 2H), 2.33 (m, 2H), 2.46 (m, 2H), 2.86 (m, 1H), 3.73−3.78 (m, 2H), 4.39 (dd, J = 9.8, 3.5 Hz, 1H), 4.68 (dd, J = 9.8, 3.5 Hz, 1H), 4.85 (m, 1H), 4.90 (d, J = 10.5 Hz, 1H), 5.30 (m, 1H), 7.29 (m, 2H), 7.45 (m, 2H), 7.50−7.54 (m, 5H), 7.55−7.64 (m, 3H), 7.67−7.71 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.1, 25.1, 25.3, 26.1, 28.6, 32.5, 33.6, 35.7, 62.9, 66.2, 72.4, 73.3, 82.4 (J = 3.4 Hz), 96.8, 100.0, 117.5, 124.6 (J = 272.6 Hz), 128.9 (J = 2.6 Hz), 129.0 (J = 10.9 Hz), 129.3 (J = 11.2 Hz), 130.5, 130.7, 131.0 (J = 11.7 Hz), 131.8 (J = 13.7 Hz), 132.8, 132.8, 134.8, 160.9, 172.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ 107.2; ^{19}F NMR (376.5 MHz, $CDCl_3$) δ − 62.8 ppm; HRMS (CI) m/z calcd for $C_{32}H_{44}IrNO_2P$ (M − BAr_F)$^+$ 698.2733, found 698.2732. Anal. Calcd for $C_{64}H_{56}BF_{24}IrNO_2P$: C, 49.24; H, 3.62; N, 0.90. Found: C, 49.65; H, 3.57; N, 0.84.

[(η^4-1,5-Cyclooctadiene)-[(*S*)-2-[(*R*)-1-((diphenylphosphino)-oxy)-2,2-dimethylpropyl]-4-isopropyl-4,5-dihyrothiazole]-iridium(I)] tetrakis[3,5-bis(trifluoromethyl)phenyl]borate [(*R*,*S*)-6a]: 80% yield; red needles (crystallized from Et_2O/hexanes, mp 165−166 °C);$[\alpha]_D^{20}$ −6.7 (c = 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.05 (d, J = 6.7 Hz, 3H), 0.84 (d, J = 7.0 Hz, 3H), 1.24 (s, 9H), 1.50 (m, 1H), 1.78 (m, 1H), 1.95−2.16 (m, 3H), 2.41 (m, 2H), 2.58 (m, 2H), 2.95 (m, 1H), 3.18 (dd, J = 12.0, 3.1 Hz, 1H), 3.29 (dd, J = 12.0, 2.6 Hz, 1H), 3.45 (m, 1H), 4.21 (dd, J = 3.1, 2.6 Hz, 1H), 5.03 (m, 1H), 5.08 (d, J = 10.4 Hz, 1H), 5.28 (m, 1H), 7.14 (m, 2H), 7.41 (m, 2H), 7.47 (m, 1H), 7.53 (m, 4H), 7.56−7.65 (m, 3H), 7.71 (m, 8H), 7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2, 19.4, 26.3, 27.1, 28.6, 30.2, 30.5, 35.1, 36.2, 42.1, 61.4, 68.3, 78.5, 88.9, 99.1, 103.3, 117.5, 124.6 (J = 272.5 Hz), 128.7 (J = 10.9 Hz), 129.0, 129.5 (J = 11.6 Hz), 131.0 (J = 11.7 Hz), 132.2 (J = 13.9 Hz), 133.6, 133.7, 132.6, 133.0, 134.8, 161.6 (J = 50.4 Hz), 181.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 105.9; ^{19}F NMR (376.5 MHz, $CDCl_3$) δ − 62.8 ppm; HRMS (CI) m/z calcd for $C_{31}H_{42}IrNOPS$ (M − BAr_F)$^+$ 700.2348, found 700.2333. Anal. Calcd for $C_{63}H_{54}BF_{24}IrNOPS$: C, 48.41; H, 3.48; N, 0.90. Found: C, 48.47; H, 3.20; N, 0.85.

Iridium-Catalyzed Hydrogenations. To a solution of the corresponding ketone in dry dichloromethane in a test tube was added 1 mol % catalyst. The tube was transferred into the autoclave. It was purged three times with nitrogen and three times with hydrogen before it was pressurized to 50 bar. The mixture was stirred at this pressure. After 24 h, the pressure was released, and it was purged five times with nitrogen. The tube was taken out, and the solvent was removed in vacuo. The crude product was cleaned by flash chromatography on SiO_2 (hexanes/ethylacetate), and ee values were determined via GC analysis [CP-Chirasil-Dex capillary column (25 m × 0.25 mm)]. GC separation conditions T_0 [3 min] = 90 °C, 1 °C/min to T = 200 °C [20 min], injector 250 °C, detector 275 °C.

(*S*)-3-Methyl-4-phenylbutan-2-one [(*S*)-8a]:[46] 98% yield; 99.4% ee; $[\alpha]_D^{20}$ +34.1 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8a**] 27.52 min, t_R [(*S*)-**8a**] 27.98 min.

(*S*)-2-Methyl-1-phenylpentan-3-one [(*S*)-8b]:[46] 99% yield; 99.1% ee; $[\alpha]_D^{20}$ +57.6 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8b**] 32.23 min, t_R [(*S*)-**8b**] 33.02 min;

(*S*)-3-Benzylpentan-2-one [(*S*)-8c]:[46] 96% yield; 99.7% ee; $[\alpha]_D^{20}$ +41.8 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8c**] = 32.65 min, t_R [(*S*)-**8c**] = 32.89 min.

(*S*)-4-(4-Methoxyphenyl)-3-methylbutan-2-one [(*S*)-8d]:[46] 93% yield; 99.1% ee; $[\alpha]_D^{20}$ +38.9 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8d**] 51.36 min, t_R [(*S*)-**8d**] 51.89 min.

(*S*)-3-Methyl-4-(*p*-tolyl)butan-2-one [(*S*)-8e]:[46] 92% yield; 99.5% ee; $[\alpha]_D^{20}$ +31.8 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8e**] 34.54 min, t_R [(*S*)-**8e**] 35.91 min.

(*S*)-3-Methyl-4-(*o*-tolyl)butan-2-one [(*S*)-8f]:[46] 99% yield; 98% ee; $[\alpha]_D^{20}$ +43.2 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8f**] 32.85 min, t_R [(*S*)-**8f**] 33.53 min.

(*S*)-2-Benzylcyclohexanone [(*S*)-8g]:[46] 99% yield; 99% ee; $[\alpha]_D^{20}$ −42.1 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8g**] 59.86 min, t_R [(*S*)-**8g**] 60.10 min.

(*S*)-2-(4-Methoxybenzyl)cyclohexanone [(*S*)-8h]:[46] 92% yield; 97% ee; $[\alpha]_D^{20}$ −40.2 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8h**] 85.18 min, t_R [(*S*)-**8h**] 85.46 min.

(*S*)-2-(2-Methylbenzyl)cyclohexanone [(*S*)-8i]:[47] 96% yield; 98% ee; $[\alpha]_D^{20}$ −38.8 (c = 1, $CHCl_3$); GC t_R [(*R*)-**8i**] 66.43 min, t_R [(*S*)-**8i**] 66.70 min.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Analytical and spectroscopic data of all catalysts and hydrogenation products as well as ORTEP plots and CIFs for the Xray structures of complexes **5** and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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